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In accordance with the rules, the words, "public limited company" may be replaced by p.l.c., plc, P.L.C. or PLC.

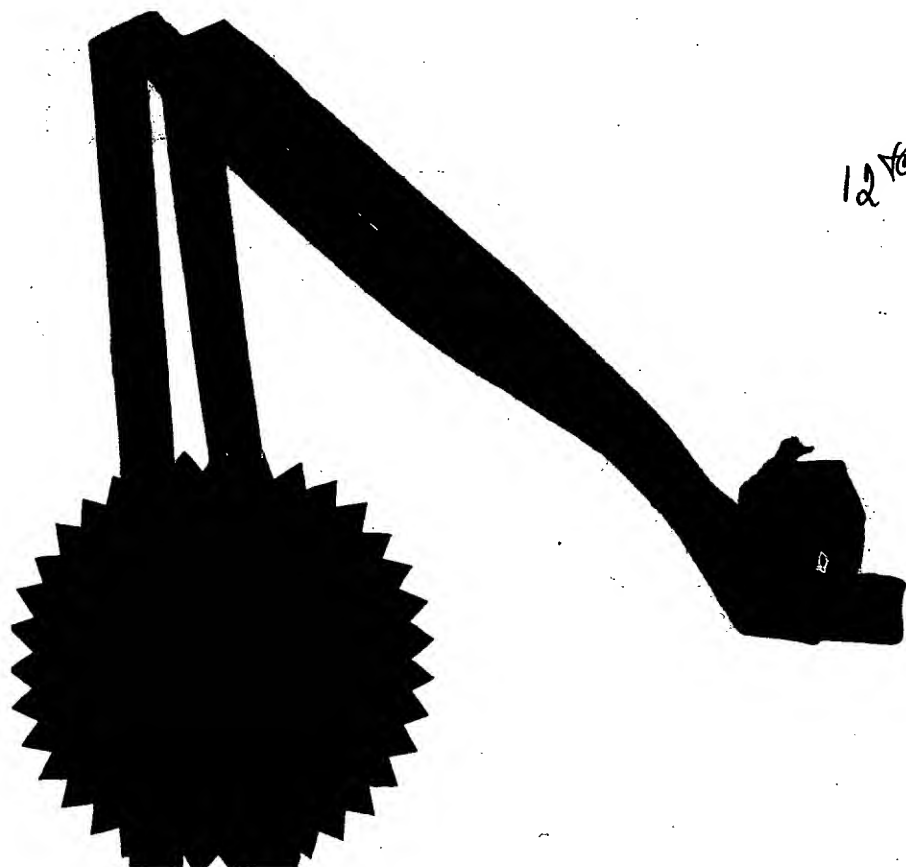
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12th day of
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W. Russell

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4 SEPT 1987

PATENTS ACT 1977

PATENTS FORM No. 1/77 (Revised 1982)

(Rules 16, 19)

The Comptroller
The Patent Office1987
20825

04/09/87 B4436 PAT*** 10.00

REQUEST FOR GRANT OF A PATENT

87 20825

THE GRANT OF A PATENT IS REQUESTED BY THE UNDERSIGNED ON THE BASIS OF THE PRESENT APPLICATION

I	Applicant's or Agent's Reference (Please insert if available)		KR/TSM/B2368
II	Title of Invention NOVEL COMPOUNDS		
III	Applicant or Applicants (See note 2)		
	Name (First or only applicant) Beecham Group p.l.c.		
	Country	United Kingdom	State ADP Code No.
	Address Beecham House, Great West Road, Brentford, Middlesex TW8 9BD, England		
	Name (of second applicant, if more than one)		
	Country State		
	Address		
IV	Inventor (see note 3)		(a) The applicant(s) is/are the sole/joint inventor(s) or (b) A statement on Patents Form No 7/77 is/will be furnished
V	Name of Agent (if any) (See note 4)	P. JONES	ADP CODE NO
VI	Address for Service (See note 5) Beecham Pharmaceuticals, Great Burgh, Yew Tree Bottom Road, Epsom, Surrey KT18 5XQ, England		
VII	Declaration of Priority (See note 6)		
	Country	Filing date	File number
VIII	The Application claims an earlier date under Section 8(3), 12(6), 15(4), or 37(4) (See note 7)		
	Earlier application or patent number and filing date		

IX Check List (To be filled in by applicant or agent)

- A The application contains the following number of sheet(s)
- 1 Request 1 Sheet(s)
- 2 Description 23 Sheet(s)
- 3 Claim(s) - Sheet(s)
- 4 Drawing(s) Sheet(s)
- 5 Abstract - Sheet(s)

- B The application as filed is accompanied by:
- 1 Priority document
- 2 Translation of priority document
- 3 Request for Search
- 4 Statement of Inventorship and Right to Grant

X It is suggested that Figure No of the drawings (if any) should accompany the abstract when published.

XI Signature (See note 8)

P. Jones
P. Jones (Miss), Chartered Patent Agent
Agent for the Applicant

NOTES:

1. This form, when completed, should be brought or sent to the Patent Office together with the prescribed fee and two copies of the description of the invention, and of any drawings.
2. Enter the name and address of each applicant. Names of individuals should be indicated in full and the surname or family name should be underlined. The names of all partners in a firm must be given in full. Bodies corporate should be designated by their corporate name and the country of incorporation and, where appropriate, the state of incorporation within that country should be entered where provided. Full corporate details, eg "a corporation organised and existing under the laws of the State of Delaware, United States of America," trading styles, eg "trading as xyz company", nationality, and former names, eg "formerly [known as] ABC Ltd." are not required and should not be given. Also enter applicant(s) ADP Code No. (if known).
3. Where the applicant or applicants is/are the sole inventor or the joint inventors, the declaration (a) to that effect at IV should be completed, and the alternative statement (b) deleted. If, however, this is not the case the declaration (a) should be struck out and a statement will then be required to be filed upon Patent Form No 7/77.
4. If the applicant has appointed an agent to act on his behalf, the agent's name and the address of his place of business should be indicated in the spaces available at V and VI. Also insert agent's ADP Code No. (if known) in the box provided.
5. An address for service in the United Kingdom to which all documents may be sent must be stated at VI. It is recommended that a telephone number be provided if an agent is not appointed.
6. The declaration of priority at VII should state the date of the previous filing and the country in which it was made and indicate the file number, if available.
7. When an application is made by virtue of section 8(3), 12(6), 15(4) the appropriate section should be identified at VIII and the number of the earlier application or any patent granted thereon identified.
8. Attention is directed to rules 90 and 106 of the Patent Rules 1982.
9. Attention of applicants is drawn to the desirability of avoiding publication of inventions relating to any article, material or device intended or adapted for use in war (Official Secrets Acts, 1911 and 1920). In addition after an application for a patent has been filed at the Patent Office the comptroller will consider whether publication or communication of the invention should be prohibited or restricted under section 22 of the Act and will inform the applicant if such prohibition is necessary.
10. Applicants resident in the United Kingdom are also reminded that, under the provisions of section 23 applications may not be filed abroad without written permission or unless an application has been filed not less than six weeks previously in the United Kingdom for a patent for the same invention and no direction prohibiting publication or communication has been given or any such direction has been received.

substituted or unsubstituted, or a substituted or unsubstituted aryl group;

R⁴ and R⁵ each represent hydrogen, or R⁴ and R⁵ together represent a bond;

A represents a benzene ring having in total up to five substituents;

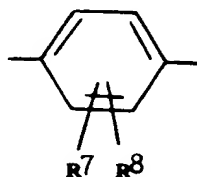
X represents oxygen, sulphur or a moiety NR⁶ wherein R⁶ represents hydrogen or alkyl; and

n represents an integer in the range of from 2 to 6.

Suitable substituents for the moiety A include halogen, substituted or unsubstituted alkyl or alkoxy.

Suitably R⁴ and R⁵ each represent hydrogen.

Suitably, A represents a moiety of formula (a):

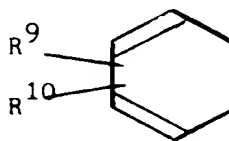


(a)

wherein R⁷ and R⁸ each independently represent hydrogen, halogen, substituted or unsubstituted alkyl or alkoxy.

Preferably, R⁷ and R⁸ each independently represent hydrogen, halogen, alkyl or alkoxy.

Suitably, R¹ and R² together represent a moiety of formula (b):



(b)

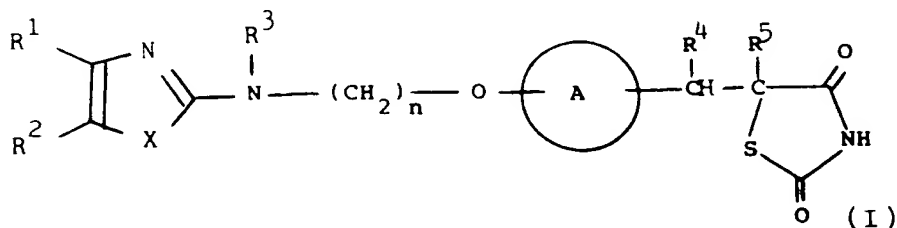
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NOVEL COMPOUNDS

This invention relates to certain novel substituted thiazole, oxazole and imidazole derivatives, to a process for preparing such compounds, to pharmaceutical compositions containing such compounds and to the use of such compounds and compositions in medicine.

It has surprisingly been discovered that certain substituted thiazole, oxazole and imidazole derivatives show good blood-glucose and blood-lipid lowering activity and are therefore of potential use in the treatment and/or prophylaxis of hyperglycaemia and hyperlipidaemia.

Accordingly, the present invention provides a compound of formula (I):



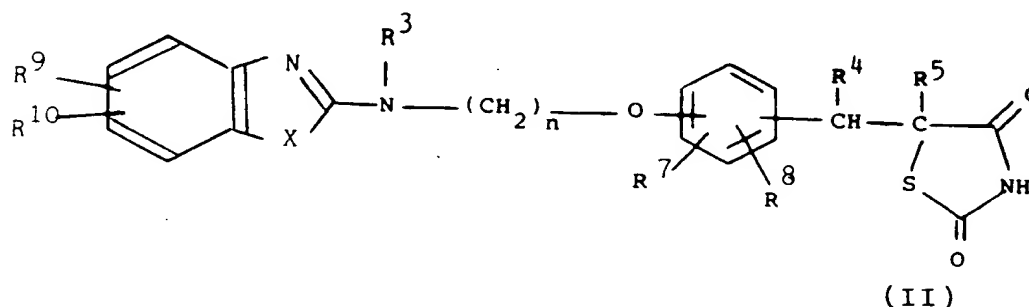
or a tautomeric form thereof, or a pharmaceutically acceptable salt thereof, wherein:

R¹ and R² each independently represents a hydrogen atom, an alkyl group or a substituted or unsubstituted aryl group or R¹ and R² together represent a residue of a benzene ring wherein each carbon atom of the residue may be substituted or unsubstituted;
 R³ represents a hydrogen atom, an alkyl group, an aralkyl group, wherein the aryl moiety may be

wherein R⁹ and R¹⁰ each independently represent hydrogen, halogen, substituted or unsubstituted alkyl or alkoxy.

Suitably, R⁹ and R¹⁰ each independently represent hydrogen, halogen, alkyl or alkoxy.

In one preferred aspect the present invention provides a class of compounds, which fall wholly within the scope of formula (I), of formula (II):



or a tautomeric form thereof, or a pharmaceutically acceptable salt thereof, wherein R³, R⁴, R⁵, X and n are as defined in relation to formula (I), R⁷ and R⁸ are as defined in relation to moiety (a) and R⁹ and R¹⁰ are as defined in relation to moiety (b).

As indicated above a compound of formula (I) may exist in one of several tautomeric forms, all of which are encompassed by the present invention.

When used herein the term 'aryl' includes phenyl and naphthyl optionally substituted with up to five, preferably up to three, groups selected from halogen, alkyl, phenyl, alkoxy, haloalkyl, hydroxy, amino,

nitro, carboxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkylcarbonyloxy, or alkylcarbonyl groups.

When used herein the term 'halogen' refers to fluorine, chlorine, bromine and iodine; preferably chlorine.

When used herein the terms 'alkyl' and 'alkoxy' relate to groups having straight or branched carbon chains, containing up to 12 carbon atoms.

Suitable alkyl groups are C₁-12 alkyl groups, especially C₁-6 alkyl groups e.g. methyl, ethyl, n-propyl, iso-propyl, n-butyl, isobutyl or tert-butyl groups.

Suitable substituents for any alkyl group include those indicated above in relation to the term 'aryl'.

Suitable pharmaceutically acceptable salts include salts of the thiazolidinedione moiety, and, where appropriate, salts of carboxy groups.

Suitable pharmaceutically acceptable salts of the thiazolidinedione moiety include metal salts especially alkali metal salts such as the lithium, sodium and potassium salts.

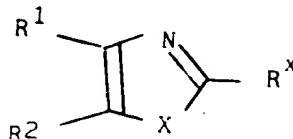
Suitable pharmaceutically acceptable salts of carboxy groups include metal salts, such as for example aluminium, alkali metal salts such as sodium or potassium, alkaline earth metal salts such as calcium or magnesium and ammonium or substituted ammonium salts, for example those with lower alkylamines such as triethylamine, hydroxy alkylamines such as

(i) converting a compound of formula (I) to a further compound of formula (I);

(ii) preparing a pharmaceutically acceptable salt of the compound of formula (I).

Suitably, R^a represents $R^3HN-(CH_2)_n-O-$ wherein R^3 and n are as defined in relation to formula (I).

Suitably, when R^a is $R^3HN-(CH_2)_n-O-$, an appropriate reagent capable of converting R^a to a moiety (c) is a compound of formula (IV):



(IV)

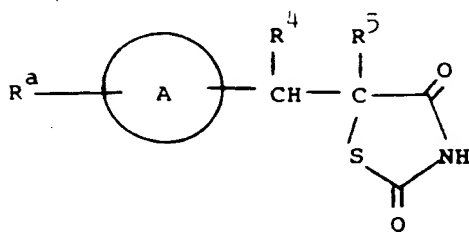
wherein R^1 , R^2 and X are as defined in relation to formula (I) and R^X represents a leaving group.

A suitable leaving group R^X includes a halogen atom, preferably a chlorine or bromine atom, or a thioalkyl group for example a thiomethyl group.

The reaction between the compound of formula (III) and the appropriate reagent may be carried out under conditions suitable to the particular compound of formula (III) and the reagent chosen; thus for example the abovementioned reaction between a compound of formula (III) wherein R^a represents $R^3HN-(CH_2)_n-O-$ and the compound of formula (IV), may be carried out in any

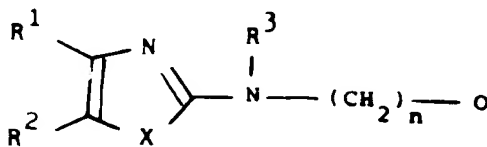
2-hydroxyethylamine, bis-(2-hydroxyethyl)-amine or tri-(2-hydroxyethyl)-amine, cycloalkylamines such as bicyclohexylamine, or with procaine, dibenzylpiperidine, N-benzyl-β-phenethylamine, dehydroabietylamine, N,N'-bisdehydroabietylamine, glucamine, N-methylglucamine or bases of the pyridine type such as pyridine, collidine or quinoline.

In a further aspect the present invention also provides a process for the preparation of a compound of formula (I), or a pharmaceutically acceptable salt thereof, which process comprises reacting a compound of formula (III):



(III)

wherein R⁴, R⁵ and A are as defined in relation to formula (I), and R^a is a moiety convertible to a moiety of formula (c):

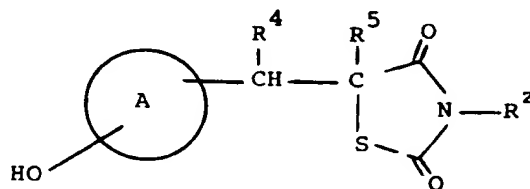


(c)

wherein R¹, R², R³, X and n are as defined in relation to formula (I), with an appropriate reagent capable of converting R^a to the said moiety (c) and thereafter, if required, carrying out one or more of the following optional steps:

Suitably, R^b is a moiety convertible to a moiety R^a , for example R^b may represent a hydroxyl group.

The moiety R^b may be converted to the moiety R^a by any suitable means, for example when R^b represents a hydroxyl group and R^a represents $R^3HN(CH_2)_nO-$ the appropriate conversion may be carried out by coupling a compound of formula (VA):



(VA)

wherein R^4 , R^5 and A are as defined in relation to formula (I) and R^Z is hydrogen or a nitrogen protecting group, with a compound of formula (VI):



(VI)

wherein R^3 and n are as defined in relation to formula (I) in the presence of a suitable coupling agent; and thereafter, if required, carrying out one or more of the following optional steps:

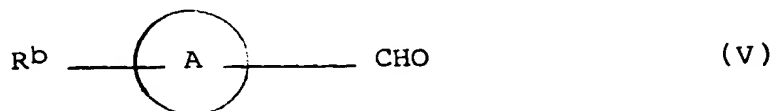
(i) reducing a compound of formula (III) wherein R^4 and R^5 together represent a bond, to a compound of formula (III) wherein R^4 and R^5 each represent hydrogen;

(ii) removing any nitrogen protecting group.

A suitable coupling agent for the coupling reaction between the compound of formula (VA) and (VI) is provided by diethylazodicarboxylate and triphenylphosphine. The coupling reaction may be

suitable solvent, for example tetrahydrofuran, at a temperature in the range of between 0 and 60°C.

A compound of formula (III) may be prepared from a compound of formula (V):



wherein A is as defined in relation to the compound of formula (I) and R^b is a moiety R^a , or a moiety convertible to a moiety R^a ; by reaction of the compound of formula (V) with 2,4-thiazolidinedione; and thereafter if required carrying out one or more of the following optional steps:

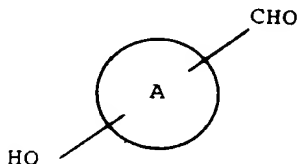
(i) reducing a compound of formula (III) wherein R^4 and R^5 together represent a bond, into a compound of formula (III) wherein R^4 and R^5 each represent hydrogen;

(ii) converting a moiety R^b to a moiety R^a .

The reaction between the compound of formula (V) and 2,4-thiazolidinedione will of course be carried out under conditions suitable to the nature of the compound of formula (V), in general the reaction being carried out in a solvent such as toluene, suitably at an elevated temperature such as the reflux temperature of the solvent and preferably in the presence of a suitable catalyst such as piperidinium benzoate. Favourably, in the reaction between the compound of formula (V) and 2,4-thiazolidinedione, the water produced in the reaction is removed from the reaction mixture, for example by means of a Dean and Stark apparatus.

carried out in any suitable solvent at a low to medium temperature, for example in tetrahydrofuran at a temperature in the range of between 0 and 60°C.

The compound of formula (VA) may be prepared by reacting a compound of formula (VII):



(VII)

wherein A is as defined in relation to formula (I), with 2,4-thiazolidinedione.

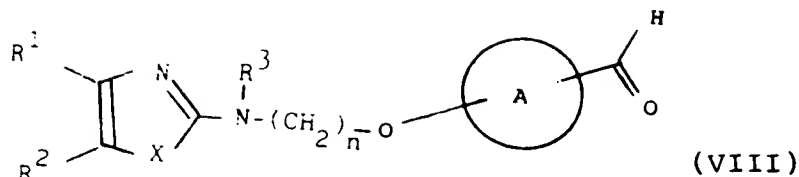
Suitable conditions for the reaction between a compound of formula (VII) and 2,4-thiazolidinedione are those defined above in relation to the reaction between the compounds of formula (V) and 2,4-thiazolidinedione.

The compounds of formula (VI) and (VII) are either known compounds or are prepared using methods analogous to those used to prepare known compounds.

Suitable protecting groups are those used conventionally in the art, the methods of formation and removal of such protecting groups being those conventional methods appropriate to the molecule being protected.

A suitable nitrogen protecting group is a benzyl group.

A compound of formula (I), or a pharmaceutically acceptable salt thereof, may also be prepared by reacting a compound of formula (VIII):

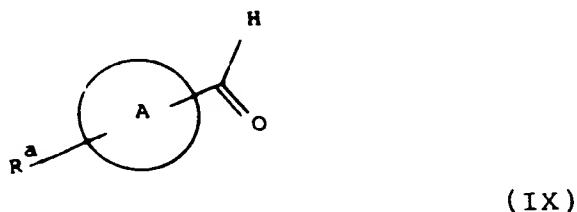


wherein R^1 , R^2 , R^3 , A, X and n are as defined in relation to formula (I) with 2,4-thiazolidinedione; and thereafter if required carrying out one or more of the following optional steps:

- (i) converting a compound of formula (I) into a further compound of formula (I);
- (ii) preparing a pharmaceutically acceptable acid addition salt of a compound of formula (I).

The reaction between a compound of formula (VIII) and 2,4-thiazolidinedione may suitably be carried out under analogous conditions to those used in the reaction between a compound of formula (V) and 2,4-thiazolidinedione.

A compound of formula (VIII) may be prepared by reacting a compound of formula (IX):



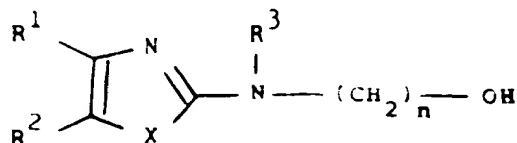
wherein A is as defined in relation to formula (I) and R^a is as defined in relation to formula (III), with an

appropriate reagent capable of converting R^a to the above defined moiety (c)

Suitable values for R^a include those described above in relation to the compound of formula (III).

Suitable reaction conditions for the reaction of the compound of formula (IX) and the appropriate reagent may include those described above in relation to the preparation of compound (III) with the said appropriate reagent.

A particularly favoured form of the process for preparing a compound of formula (VIII) from a compound of formula (IX) is that wherein R^a represents a leaving group, preferably a fluorine atom, and the appropriate reagent is a compound of formula (X):



(X)

wherein R^1 , R^2 , R^3 , X and n are as defined in relation to formula (I).

The reaction between the compounds of formulae (VIII) and (X) may be carried out under any suitable conditions, for example in a solvent such as dimethylsulphoxide at an elevated temperature for example in the range of between 100 to 150°C, suitably in the presence of a base such as potassium carbonate.

The compounds of formula (IX) are known compounds or compounds prepared by methods analogous to those used

to prepare known compounds, for example
4-fluorobenzaldehyde is a known commercially available
compound.

A compound of formula (X) may be prepared by reacting a
compound of the hereinabove defined formula (IV), with
a compound of the hereinbefore defined formula (VI).

The reaction between the compounds of formula (IV) and
(VI) may be carried out under any suitable conditions,
such as in solvent, for example tetrahydrofuran, at a
low to medium temperature, for example a temperature in
the range of between 0 and 60°C.

Favourably, when R³ represents hydrogen the reaction is
carried out using the compound of formula (VI) as a
solvent at a low to elevated temperature, suitable an
elevated temperature such as in the range of between
100 and 170°C.

The abovementioned conversion of a compound of formula
(I) into a further compound of formula (I) includes the
following conversions:

(a) reducing a compound of formula (I) wherein R⁴
and R⁵ together represent a bond, to a compound of
formula (I) wherein R⁴ and R⁵ each represent hydrogen;
and

(b) converting a compound of formula (I) wherein R⁶
represents hydrogen into a compound of formula (I)
wherein R⁶ represents an alkyl group.

The conversion of a compound of formula (I) to a
further compound of formula (I) may be carried out by
using any suitable method.

Thus the present invention provides a compound of formula (I), or a pharmaceutically acceptable salt thereof, for use in the treatment of and/or prophylaxis of hyperglycaemia.

In a further aspect the present invention also provides a compound of formula (I), or a pharmaceutically acceptable salt thereof, for use in the treatment and/or prophylaxis of hyperlipidaemia.

A compound of the general formula (I), or a pharmaceutically acceptable salt thereof, may be administered per se or, preferably, as a pharmaceutical composition also comprising a pharmaceutically acceptable carrier.

Accordingly, the present invention also provides a pharmaceutical composition comprising a compound of the general formula (I), or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier therefor.

As used herein the term 'pharmaceutically acceptable' embraces compounds, compositions and ingredients for both human and veterinary use: for example the term 'pharmaceutically acceptable salt' embraces a veterinarily acceptable salt.

The composition may, if desired, be in the form of a pack accompanied by written or printed instructions for use.

Usually the pharmaceutical compositions of the present invention will be adapted for oral administration, although compositions for administration by other routes, such as by injection and percutaneous

A suitable reduction method for the abovementioned conversion (a) includes catalytic reduction or the use of a metal/solvent reducing system.

Suitable catalysts for use in the catalytic reduction are palladium on carbon catalysts, preferably a 10% palladium on charcoal catalyst; the reduction being carried out in a solvent, for example dioxan, suitably at ambient temperature.

Suitable metal/solvent reducing systems include magnesium in methanol.

In the abovementioned conversion (b), the compound of formula (I) wherein R^6 represents hydrogen may be converted into a further compound of formula (I) wherein R^6 represents alkyl by treating the appropriate compound of formula (I) with a suitable alkylating agent, for example an alkyl halide, preferably an alkyl iodide.

The abovementioned reduction of a compound of formula (III) wherein R^4 and R^5 together represent a bond to a compound of formula (III) wherein R^4 and R^5 each represent hydrogen, may be carried out under analogous conditions to those referred to above in conversion (a) of the compound of formula (I).

It will be appreciated that in the abovementioned conversions (a) and (b), any reactive group in the compound of formula (I) would be protected, according to conventional chemical practice, where necessary.

The present invention also provides a compound of formula (I), or a pharmaceutically acceptable salt thereof, for use as an active therapeutic substance.

absorption are also envisaged.

Particularly suitable compositions for oral administration are unit dosage forms such as tablets and capsules. Other fixed unit dosage forms, such as powders presented in sachets, may also be used.

In accordance with conventional pharmaceutical practice the carrier may comprise a diluent, filler, disintegrant, wetting agent, lubricant, colourant, flavourant or other conventional adjuvant.

Typical carriers include, for example, microcrystalline cellulose, starch, sodium starch glycollate, polyvinylpyrrolidone, polyvinylpolypyrrolidone, magnesium stearate, sodium lauryl sulphate or sucrose.

Most suitably the composition will be formulated in unit dose form. Such unit dose will normally contain an amount of the active ingredient in the range of from 0.1 to 1000 mg, more usually 0.1 to 500 mg, and more especially 0.1 to 250 mg.

The present invention further provides a method for the treatment and/or prophylaxis of hyperglycaemia in a human or non-human mammal which comprises administering an effective, non-toxic, amount of a compound of the general formula (I), or a pharmaceutically acceptable salt thereof, to a hyperglycaemic human or non-human mammal in need thereof.

The present invention further provides a method for the treatment of hyperlipidaemia in a human or non-human mammal, which comprises administering an effective, non-toxic, amount of a compound of the general formula (I), or a pharmaceutically acceptable salt thereof, to

a hyperlipidaemic human or non-human mammal in need thereof.

Conveniently, the active ingredient may be administered as a pharmaceutical composition hereinbefore defined, and this forms a particular aspect of the present invention.

In the treatment and/or prophylaxis of hyperglycaemic humans, and/or the treatment and/or prophylaxis of hyperlipidaemic human, the compound of the general formula (I), or a pharmaceutically acceptable salt thereof, may be taken in doses, such as those described above, one to six times a day in a manner such that the total daily dose for a 70 kg adult will generally be in the range of from 0.1 to 6000 mg, and more usually about 1 to 1500 mg.

In the treatment and/or prophylaxis of hyperglycaemic non-human mammals, especially dogs, the active ingredient may be administered by mouth, usually once or twice a day and in an amount in the range of from about 0.025 mg/kg to 25 mg/kg, for example 0.1 mg/kg to 20 mg/kg. Similar dosage regimens are suitable for the treatment and/or prophylaxis of hyperlipidaemia in non-human mammals.

The present invention also provides the use of a compound of formula (I), or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment and/or prophylaxis of hyperglycaemia.

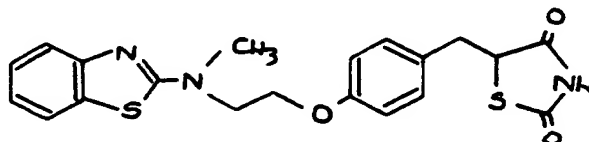
The present invention further provides the use of a compound of formula (I) or a pharmaceutically acceptable salt thereof, for the manufacture of a

medicament for the treatment and/or prophylaxis of
hyperlipidaemia.

The following Examples illustrate the invention but do
not limit it in any way.

EXAMPLE 1

5- {4-[2-(N-methyl-N-(2-benzothiazolyl)amino)ethoxy]benzyl}
2,4-thiazolidinedione.



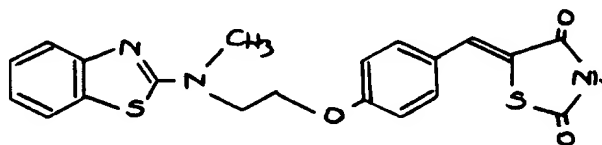
5- {4-[2-(N-methyl-N-(2-benzothiazolyl)amino)-ethoxy]benzylidene}
2,4-thiazolidinedione (2g) in dry 1,4-dioxan (70ml) was reduced
under hydrogen in the presence of 10% palladium on charcoal (3g)
at ambient temperature and atmospheric pressure until hydrogen
uptake ceased. The solution was filtered through diatomaceous
earth, the filter pad was washed exhaustively with dioxan and the
combined filtrates were evaporated to dryness under vacuum. The
title compound (m.p. 167-8°C) was obtained after crystallisation
from methanol.

¹H NMR (DMSO-d₆)

2.9-3.4 (2H, complex); 3.25 (3H,s); 3.9 (2H, complex); 4.25 (2H,
complex); 4.8 (1H, complex); 6.8-7.75 (8H, complex) 12.0 (1H, s,
exchanges with D₂O).

EXAMPLE 2

5- {4-[2-(N-methyl-N-(2-benzothiazolyl)amino)ethoxy]-benzylidene}-
2,4-thiazolidinedione.



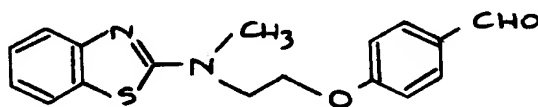
A solution of 4-[2- { N-methyl-N-(2-benzothiazolyl)amino } ethoxy] benzaldehyde (1.9g) and 2,4-Thiazolidinedione (0.8g) in toluene (100ml) containing a catalytic quantity of piperidinium acetate was boiled under reflux in a Dean and Stark apparatus for 2 hours. The mixture was cooled and filtered and the filtered solid was dried to give the title compound (2.0g) mp 219°C.

¹H NMR (DMSO -d₆)

3.2 (3H, s); 3.9 (2H, t); 4.35 (2H, t); 6.8-7.7 (10H, Complex).

EXAMPLE XI

4-[2-{N-methyl-N-(2-benzothiazolyl)amino}ethoxy]-benzaldehyde.



A mixture of 4-fluorobenzaldehyde (1.5g) and 2- N-methyl-N-(2-benzothiazolyl) aminoethanol (2.4g) in DMSO (50ml) containing anhydrous potassium carbonate (2g) was stirred at 100°C for 24 hours. The mixture was cooled to room temperature and added to water (300ml). The aqueous solution was extracted with diethyl ether (2x300 ml). The organic extracts were washed with brine (1x300 ml), dried (MgSO₄), filtered and evaporated to dryness. The title compound was obtained as a waxy solid following chromatography on silica-gel in 1% methanol dichloromethane.

¹H NMR (CDCl₃)

3.2 (3H, s); 3.8 (2H, t); 4.2 (2H, t); 6.8-7.8 (8H, Complex); 9.8 (1H, s).

DEMONSTRATION OF EFFICACY OF COMPOUNDS

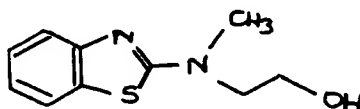
Obese Mice, Oral Glucose Tolerance Test.

C57bl/6 obese (ob/ob) mice were fed on powdered oxoid diet. After at least one week, the mice continued on a powdered oxoid diet or were fed powdered oxoid diet containing the test compound. After 8 days on the supplemented diet all of the mice were fasted for 5 hours prior to receiving an oral load of glucose (3 g/kg). Blood samples for glucose analysis were taken 0, 45, 90 and 135 minutes after glucose administration and the results appear below as the percentage reduction in area under the blood glucose curve where test compound treated groups are compared with the control groups. 7 mice were used for each treatment.

EXAMPLE NO:	LEVEL IN DIET ($\mu\text{mol kg}^{-1}$ of DIET)	%REDUCTION IN AREA UNDER BLOOD GLUCOSE CURVE
1	100	51

EXAMPLE X2

2-{N-methyl-N-(2-benzothiazolyl)} aminoethanol



A mixture of 2-chlorobenzothiazole (8.5g) and 2-methylaminoethanol (20 ml) was heated at 120°C under pressure in a sealed, glass lined, stainless steel reaction vessel for 18 hours. After cooling, the oil was added to water (100ml), extracted with dichloromethane (2x100 ml), the organic extracts were dried (MgSO₄), filtered and evaporated to dryness. Chromatography of the residual oil on silica-gel in 2½% methanol-dichloromethane gave the title compound which was used in the next stage without further purification.

¹H NMR (CDCl₃)

3.15 (3H, s); 3.4-4.0 (4H, m); 4.7 (1H, broad s, exchanges with D₂O); 6.8-7.6 (4H, complex).

Toxicology

No toxicological effects were indicated for any of the compounds of the invention in any of the abovementioned tests.

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